UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/826,069	04/04/2001	Yaakov Naparstek	56040-B/JPW/GJG/CSN	3884

62433 7590 12/31/2007

EDWARD LANGER
c/o SHIBOLETH YISRAELI ROBERTS ZISMAN & CO.
1 PENN PLAZA-SUITE 2527
NEW YORK, NY 10119

EXAMINER	
EWOLDT, GERALD R	
ART UNIT	**PAPER NUMBER**
1644	
MAIL DATE	**DELIVERY MODE**
12/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/826,069	NAPARSTEK, YAAKOV	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2007 and 10 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 9/24/07 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's remarks and declarations filed 9/24/07 and 12/10/07 have been entered.

2. Claims 8-14, are being acted upon.

3. As set forth previously, the priority date of the instant application is its filing date, 4/04/2001.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 8-14 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Gaubitz et al. (1999) in view of U.S. Patent No. 6,228,363 and Madaio et al. (1996).

As set forth previously, Gaubitz, M., et al. teaches a method of treating lupus comprising extracorporeal column immunoadsorption of a subject's plasma for the removal of pathogenic antibodies. The reference further teaches that dsDNA-Ab play a "pivotal" role in the pathogenesis of SLE and that their removal proved useful for the treatment of the disease (see particularly Introduction and Discussion).

The reference teaching differs from the claimed invention only in that it does not teach a method employing a column comprising the R38 peptide nor the use of a Sepharose™ column.

The '363 patent teaches that the R38 peptide is derived from laminin and is recognized by pathogenic lupus antibodies (see particularly column 3, lines 13-19).

Madaio et al. teaches that dsDNA-Ab from lupus patients also recognize laminin (see particularly Abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform a method of treating lupus comprising extracorporeal column immunoadsorption of a subject's plasma for the removal of pathogenic antibodies, as taught by Gaubitz et al., employing the R38 peptide of the '363 patent. One of ordinary skill in the art at the time the invention was made would have been motivated to employ the R38 peptide on an immunoadsorption column given the teachings of Madaio et al. that dsDNA-Ab from lupus patients also recognize laminin and the '363 patent that the R38 peptide is derived from laminin and is recognized by pathogenic lupus antibodies. Note that Claim 8 is included in the rejection because various types of immunoadsorber matrices (including Sepharose™) for column chromatography were well-known in the art at the time of the invention. The choice of any particular immunoadsorber matrix would have comprised only routine optimization of the claimed method and would have been well within the purview of one of ordinary skill in the art at the time of the invention. Note that new claim 10 does not recite any new limitations because all ligands are coupled to Sepharose™ in some sort of "coupling buffer" (an ordinarily skilled artisan would know that Sepharose™ could not used in a dry form for column chromatography because column chromatography employs the flow of liquid through the column).

Applicant's arguments, filed 9/24/07, have been fully considered but they are not persuasive. Applicant argues a lack of expectation of success with the method of the combined references.

As stated in the rejection, the extracorporeal column immunoadsorption of a subject's plasma for the removal of pathogenic antibodies was known in the art. Substituting a ligand known to bind said pathogenic antibodies for the ligand of the primary reference would have been expected function for the binding and removal of said pathogenic antibodies from the plasma.

Applicant argues unexpected results and further argues unexpected results need not be disclosed in the specification.

It is well established that the assertion of unexpected properties in the course of prosecution is not as persuasive as when said results are disclosed in the specification. As set forth in *In re Davies and Hopkins* 177 USPQ 381 (CCPA 1973), the court held that evidence alleging unexpected properties need not be considered after filing because it properly belonged in the specification as filed:

"There is no specific statutory requirement that compels applicant to disclose all properties of chemical compounds or compositions in his application; insofar as statute is

concerned, only disclosure requirements are in first paragraph of 35 U.S.C. 112; however, public will derive the most benefit from a patent when it discloses on its face those properties or utilitarian advantages which were ultimately persuasive on question of nonobviousness".

While a case of *prima facie* obviousness can be rebutted by a showing of unexpected results, said results properly belong in the specification. Much the same as in this case, the court stated:

"Apparently it was only in the face of the rejections based on this art that appellants were moved to attempt to distinguish the properties obtained using the copolymer as a toughening agent versus using a homopolymer of butadiene".

The court concluded:

"Nevertheless, the public will derive the most benefit from a patent when it discloses on its face those properties or utilitarian advantages which were ultimately persuasive on the question of nonobviousness. However, when, as here, an applicant has satisfied the requirements of § 112, we would be reluctant to require him to disclose more unless it could be done without prejudice to him. But if the applicant can be required to include the properties in his specification without prejudice to him, a compromise is reached upon which the evidentiary ruling can be based".

Further, a proper showing of unexpected results would also include both statistical evidence and a comparison to the most closely related prior art, neither of which are provided here.

Applicant cites the 9/17/07 1.132 declaration of Inventor Naparstek.

The Inventor states in paragraph 8 that the claimed method has been performed on two patients and that in a single patient, "As shown in Figure 12, the level of anti-VRT (R38) antibodies decreased after the Luposorb™ apheresis and returned to the original levels after more than 5 weeks." In paragraph 10 the Inventor states, "As stated in paragraph 8 above, the continuing decline in antibody levels is an unusual and unexpected result, one that could not have been predicted from the disclosure of any of the references cited, nor any reference known to me".

First note that the Inventor's statements are unclear and confusing in that paragraph 10 refers to a conclusion that is not drawn in paragraph 8. Regardless, a review of the data of Figure 12 reveals that it is not statistically significant and thus is of questionable probative value. Further, there is no comparison to the closest prior art and no showing that the decline in antibody levels is actually unexpected. Finally note that it appears that a rebound effect is demonstrated wherein antibody levels are actually higher at day 58 than they were pretreatment. If said data were to be found to be persuasive said data might necessitate a rejection for lack of enablement.

Applicant cites the additional 1.132 declaration of Inventor Naparstek of 12/10/07.

The Inventor cites two references, Gokhale et al. and Grainger et al., to argue that an antibody rebound effect often follows plasmapheresis. The Inventor further argues that the rebound effect was not seen with the method of the instant claims.

As set forth in Grainger et al. the antibody rebound effect after the removal of all antibodies from a subject's plasma has been observed previously. Thus, sound scientific reasoning and common sense would dictate that improved plasmapheresis methods would seek to avoid this effect. Clearly, the concept of removing only pathogenic antibodies from a subject's plasma comprises the next logical step and does not require great insight. Thus, the claimed method would have been obvious to the ordinarily skilled artisan at the time of the invention.

The value of post-filing results submitted only in an attempt to overcome an obviousness rejection has been discussed above. Further regarding the instant results, however, it is unclear whether or not the antibody rebound effect is actually avoided with the method of the instant claims. Note that the effect was not seen in the patient of the Inventor's 9/17/07 declaration until day 58 post plasmapheresis. In the data of the instant declaration the post treatment antibody levels are disclosed only after "one month". Accordingly, it is unclear what the antibody levels might rise to after two months or longer.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter written description rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, the method as broadly claimed further encompassing the *in vivo* administration of the R38 peptide which is not supported by the instant specification. Note: in the Final Action of 9/08/07 a typographical error indicated that Claim 11 was rejected.

Applicant cites pages 4 and 11 and Figures 5, 6, 7, and 9 for support.

Page 4 of the specification discloses only that the R38 peptide is recognized by pathogenic antibodies and might therefore be used in a method of treatment. Page 11 and the figures disclose results of specific experiments, indeed the experiment at page 11 employs a mouse model of SLE. Clearly, these cites do not support the broad method of the claim which even encompasses the administration of the R38 peptide to humans.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's

voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

10. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

12/22/07

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600